A METHOD FOR CLEANING THE COLON FOR EXAMINATION

[0001] The instant application is a continuation-in-part of co-pending U.S. patent application Serial No. 10/194,251, filed July 15, 2002.

BACKGROUND

[0002] The invention relates to a method for rapid bowel cleansing which is particularly useful for preparing the bowel prior to surgery or diagnostic procedures such as colonoscopies.

Field

[0003] Gastrointestinal agents for regulating bowel movement can conveniently be placed into two categories: laxatives and bowel cleansers. Laxatives are formulated for long-term use, with the intention of eliminating constipation and obtaining a regular bowel function. Many laxatives work by stimulating bowel motility (peristalsis) in various ways, as by distending the gut with bulking or osmotic agents, or by directly stimulating the bowel nerves or muscles with stimulant laxatives. Other laxatives function as stool softeners or lubricants. The various types of laxatives are often combined in attempts to maximize efficacy or to reduce side effects of the agents.

[0004] Bowel cleansers, also called purgatives, cathartics, and lavages, are formulated for rapid emptying of the bowel and are intended for short-term use only. They are commonly used as "bowel preps" for emptying the bowel prior to surgery, childbirth, or diagnostic procedures, and usually comprise an osmotic or stimulant administered by either oral or anal route. While purgatives formulated for patient use as enemas are often prescribed before examinations, they are awkward to handle and are

frequently not properly administered, so orally-administered preparations are generally preferred. However, the orally-administered compositions for rapid bowel cleansing in common use also have disadvantages which discourage patient compliance.

[0005] The most commonly prescribed oral bowel preps today for bowel examination comprise sodium phosphate compositions in varying proportions of monobasic and dibasic species, and polyethylene glycol (PEG) in combination with electrolytes.

[0006] Sodium phosphate is a saline osmotic laxative, sold, for example, as Fleet Phospho-Soda® (C.B. Fleet Co., Lynchburg, Virginia), which contains both mono- and dibasic uncoated sodium phosphate powders. Sodium phosphate is also sold as Visicol™, which comprises monobasic and dibasic sodium phosphates in tablet form. This laxative, when formulated and used as a bowel cleanser, is associated with nausea, vomiting, and symptoms of electrolyte imbalance; the product also has an unpleasant taste. As a result, patient compliance is difficult to obtain, particularly when the cleanser is supplemented with, for example, another saline agent such as a magnesium salt, or a bowel stimulant such as bisacodyl.

[0007] While PEG is known for its successful use as a long-term osmotic laxative in combination with dietary fiber (as described in U.S. Patent 5,710,183, issued January 20, 1998 to Halow, and incorporated herein by reference), PEG purgatives such as Colyte® (Braintree Laboratories, Braintree, MA) have poor patient compliance. They have an unpleasant taste, and the amount and frequency of fluid the patent is required to drink, typically 8 fluid ounces every ten minutes over several hours, frequently cause severe bloating and attendant nausea. Further, although these

purgatives normally include electrolytes to counterbalance electrolyte loss during treatment, symptoms of electrolyte imbalance are, notwithstanding, often experienced by the patient.

SUMMARY

[0008] The method disclosed herein provides a clean colon for examination through the use of polyethylene glycol; dibasic sodium phosphate; and, optionally, monobasic sodium phosphate; which are dissolved in an aqueous carrier prior to use.

[0009] The disclosed invention further provides methods for the short-term use of the compositions as cathartics, or as preparations used prior to surgery, bowel examinations, childbirth, or similar occasions.

[0010] Because of the relatively low volume of liquid to be ingested and relatively fast action of the method disclosed herein, use of the disclosed method provides a clean colon suitable for examination without inducing an osmotic imbalance in the colon. Therefore, it is not necessary to use electrolytes with the PEG/sodium phosphate solution to prevent an osmotic imbalance in the colon.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIGURES 1-6 are photographs taken during a colonoscopy of six different patients clean-out of various sections of the colon using the disclosed method.

DETAILED DESCRIPTION OF THE EMBODIMENTS

[0012] Polyethylene glycols useful in the method of the disclosed invention broadly include any food-grade or pharmaceutical-grade PEG. Currently preferred for convenience of use in the disclosed method are polymers having molecular weights above about 900 Daltons which are solid at room temperature and soluble in or miscible

with water. Polymers having average molecular weights between about 3000 Daltons and about 8000 Daltons are exemplary. Both PEG 4000, which is nearly odorless and tasteless and widely available in USP grade, and PEG 3350, are suitable for use in the disclosed method. A proprietary laxative, sold under the brand MiraLax® (Braintree Laboratories, *supra*), is also a useful source of PEG 3350 powder. MiraLax® laxative is readily soluble in water. Still other suitable PEG powders are commercially available, such as from the Spectrum Chemical Mfg. Company, Gardena, CA. Non-powdered PEG should be comminuted to a particle size that is readily soluble in or miscible with water before use.

[0013] The sodium phosphate powder according to the invention comprises a pharmaceutical-grade (USP) free flowing powder of anhydrous dibasic sodium phosphate (Na_2HPO_4, disodium phosphate), optionally in combination with monobasic sodium phosphate monohydrate ($NaH_2PO_4 \cdot H_2$), monosodium phosphate), or anhydrous, such as conventionally used in saline laxatives, for example, the powders described in the Fleet Phospho-Soda® composition discussed *supra*. The disclosed sodium phosphate powder enables the disclosed method with a saline osmotic effect which stimulates short-term hyper-motility of the intestines. This hyper-motility of the intestines causes fecal matter to move through the bowels. The sodium phosphate powder complements the effect of the PEG component and is used in amounts which provide the desired osmolarity for this purpose, as known in the art. It is the use of PEG in the disclosed method which maintains the hyper-motility of the intestines started by the sodium phosphate powder. This maintenance of the hyper-motility of the intestines assures a clean bowel for examination.

[0014] To enable the step of administering the disodium phosphate and PEG to the patient, the combination of the sodium phosphate powder and the PEG powder is simply dissolved by mixing into any desired aqueous carrier, such as water or juice.

[0015] The PEG powder and the sodium phosphate powder are combined in amounts which provide a composition that will first stimulate hypermotility in the bowel then maintain this hypermotility which preferably will evacuate the bowel in the course of a few (3-4) hours. It has been found that compositions ranging from at least about 50% to about 90% by weight of PEG powder and from at least about 10% to about 50% by weight of sodium phosphate powder, based on the combined weight of the sodium phosphate powder and the PEG powder combination provide satisfactory results. Typically, a dry bowel examination preparation composition for use in the disclosed method will contain about 60 to about 80% by weight of PEG powder and about 20 to about 40% by weight of sodium phosphate powder. The term sodium "phosphate powder" as used herein refers to either disodium phosphate powder alone, or disodium phosphate powder in combination with monosodium phosphate powder.

[0016] In another typical implementation of the disclosed method, the amount of PEG powder will be about 70 to about 80% by weight, and about 20 to about 30% by weight sodium phosphate powder, based on the total weight of the combination of PEG powder and sodium phosphate powder. The combined PEG powder and the sodium phosphate powder should make up no less than about 80% by weight of a composition containing additives for optimum results. Use of combinations containing about 75 to about 80% by weight PEG powder and about 20 to about 25% by weight sodium phosphate powder in the disclosed method are preferred for most applications.

However, under some circumstances it may be desirable to use amounts of PEG powder at the high end of the range (e.g., from above about 80% to about 90% by weight) with a concomitant decrease of sodium phosphate powder to below about 20% by weight to about 10% by weight, for example to obtain a more rapid bowel cleanout. Conversely, under some circumstances, amounts of sodium phosphate powder at the high end of the range (e.g., from above about 40% to about 50% by weight) with a decrease in the amount of PEG powder to below about 60% to about 50% by weight may be desirable. Generally, at least a major amount (greater than about 50% by weight) of the sodium phosphate powder present is disodium phosphate. If monosodium phosphate is included with the disodium phosphate, the monosodium phosphate should usually make up less than one-half, and preferably less than one-quarter, of the combination of the monosodium phosphate and the disodium phosphate.

[0017] To formulate a convenient single dosage drink for use in the disclosed method, a combination of dry powders is made which contains about 45 grams to about 130 grams PEG powder and from about 5 grams to 45 grams sodium phosphate powder, preferably from about 45 grams to about 70 grams powdered PEG and 10 to 30 grams phosphate powder. Acceptable results from use of the disclosed method were obtained from use of about 55 grams to about 65 grams PEG and about 15 grams to about 25 grams sodium phosphate powder, ~~is~~ dissolved or suspended in an aqueous liquid of choice, such as water, tea, or juice.

[0018] The sodium phosphate powder should be readily soluble in the aqueous drink medium to promote optimum palatability and patient compliance. Reduced-solubility sodium phosphate powders such as sodium phosphate powders coated with

insoluble materials are not recommended. Suitable sodium phosphate powders for use in the practice of the present invention include the water-soluble free-flowing untreated sodium phosphate powders described and exemplified *supra* as mono- and di-sodium phosphate powders commonly used in this art.

[0019] In an exemplary drink formulation, a single dose dry prep composition containing from about 58 grams to about 63 grams PEG powder and from about 15 grams to about 20 grams sodium phosphate powder, for example, about 60 grams powdered PEG powder and about 18 grams sodium phosphate powder, preferably disodium phosphate powder, is dissolved in about 1 quart to about 1.5 quarts of water or other aqueous liquid, for oral ingestion. Alternatively, the combination of PEG powder and sodium phosphate powder can be dissolved in a smaller portion of water, such as about eight fluid ounces. The remainder of the about 1 quart to about 1.5 quarts of water is then taken in conjunction with this solution of the powders and the about eight fluid ounces of water. The amount of water or other aqueous medium in which the combination of the PEG powder and the sodium phosphate powder is dissolved or which is taken with the combination of the PEG powder and the sodium phosphate powder is not critical. However, for optimum bowel cleansing, at least about a pint of water or other aqueous medium should be used, and preferably at least a quart of water or other aqueous medium, depending upon the patient's total liquid intake during the execution of the disclosed method.

[0020] In another embodiment of the method of the invention, lower molecular weight PEG polymers such as PEG 400 which are liquid at room temperature may be used in lieu of the above powdered PEG polymers as long as they are used in the same

proportions by weight, and the sodium phosphate powder dissolved therein. If desired, the solution of liquid PEG and sodium phosphate powder may then be diluted to taste with an aqueous liquid.

[0021] The single dosage drinks including the PEG/sodium phosphate combination used in the disclosed method are taken from twice per day to four times per day on the day preceding the colonoscopy or other procedure, depending upon the degree of bowel clean-out required and the presence of complicating bowel conditions such as constipation. Typically, in an average patient, a method including the administration of two single dosage drinks twice per day for one day will provide the desired level of bowel clean-out. If, for example, the patient has not obtained satisfactory result with a prior art bowel clean-out method, use of the disclosed method for two days is recommended. Preferably, the patient will be restricted to a clear liquid diet while on the regimen, i.e., a clear liquid diet of liquids containing no significant solid material. Suitable clear liquids for a clear liquid diet include apple juice, tea, plan Jello®, 7-Up®, Sprite®, and chicken or beef broth. If the patient receives a sufficient amount of liquids which contain sodium and potassium ions to satisfy hunger, no supplemental electrolytes need to be used with the PEG/sodium phosphate combination disclosed herein. No electrolytes need to be added to correct an osmotic imbalance. The purpose of the clear liquid in the clear liquid diet is to hydrate the patient so as not to obscure pathological features present in the colon during examination.

[0022] The disclosed method may include taking the PEG/sodium phosphate in combination with conventional additives such as flavoring or coloring agents. Additionally, psyllium or other fiber commonly used as a stool-bulking agent may be

optionally added to or taken with the PEG/sodium phosphate combinations, both for its laxative properties and its potential ability to counteract any adverse effects of the other components. Kits containing single dosage drinks may include optional adjuvants such as flavor packets, dietary powders such as powdered bouillon, or herbal preparations.

EXAMPLES

Methods and Materials:

[0023] Patients were asked to prepare for a colonoscopy by ingesting about 60 grams PEG powder and about 18 grams of a sodium phosphate powder including all disodium phosphate. Each patent was given two single-dose packets of the described combination for self-administration on the day preceding the colonoscopy, with instructions to dissolve each single dose packet in water and then drink the first dose at 10 a.m. and drink the second dose at 4 p.m. For each patient, a clear liquid diet was prescribed for the day the powders in the single-dose packets were ingested. A flavor packet containing powdered Crystal Light® Ice Tea was provided to each patient for use, as desired, with the single-dose packet to encourage drinking.

Results:

[0024] The results reported here are representative of those obtained from the patients in the experimental group.

Patient #1:

[0025] The patient was a 61 year-old female with weight loss and decrease in appetite. She underwent a clear liquid diet the day before ingesting the single-dose packets at 10 a.m. and at 4 p.m. Satisfactory clean-out of the colon was observed by an adequate view of the colon verified with multiple photographs taken during the

colonoscopy. The patient had no complaints of cramping or complaints of nausea; however the patient expressed a mild dislike of the taste.

View of transverse colon of Patient #1 appears at Figure 1.

Patient #2:

[0026] The patient was an 86 year-old female with a history of anemia who used the disclosed method by taking a single-dose packet twice the day before examination along with a clear liquid diet. There was adequate bowel clean-out which presented a good view of the entire colon with no abnormalities found in the colon.

View of transverse colon of Patient #2 appears at Figure 2.

Patient #3:

[0027] The patient was a 62 year-old male with hemorrhoidal bleeding and diarrhea before undergoing a colonoscopy. The single-dose packets were taken at 10 a.m. and 4 p.m. the day before the colonoscopy and a clear liquid diet was prescribed. The patient had no complaints of nausea, vomiting, or discomfort. No complaints of taste abnormalities were made. A flavor packet was given to the patient to use as needed.

View of sigmoid colon of Patient #3 appears at Figure 3.

Patient #4:

[0028] The patient, a 74 year-old male with a history of colon polyps was being made ready for a surveillance colonoscopy. The patient used the disclosed method for bowel prep and bowel clean-out the day before the colonoscopy by using the disclosed method at 10 a.m. and 4 p.m. with one Dulcolax 10 milligram tablet. Adequate bowel clean-out revealed diverticulosis in the sigmoid colon. Mild rectal irritation and

inflammation with a good view of the entire colon was recorded by photographs taken during the colonoscopy. Tolerance of the disclosed method was reported with a slight complaint about taste. No cramping sensation was reported. No nausea and vomiting, experienced with other bowel clean-out methods, was reported.

View of descending colon of Patient #4 appears at Figure 4.

Patient #5:

[0029] The patient was a 50 year-old female who underwent surveillance colonoscopy because of a first degree relative with colon cancer. The patient ingested the single-dose packets at 10 a.m. and 4 p.m. the day before the surveillance colonoscopy. Some stool was found in the sigmoid colon. There was no liquid. It was possible to suction out the colon completely to obtain a good visualization of the entire colon verified by photographs taken during the colonoscopy. No complaints of product tolerance were made by the patient. No nausea, no vomiting, no diarrhea, and no cramping sensation were reported by the patient.

View of transverse colon of Patient #5 appears at Figure 5.

Patient #6:

[0030] The patient was a 50-year old female with continuing diarrhea. A colonoscopy was used to look for a possible cause of the diarrhea. The single-dose packets were taken at 10 a.m. and 4 p.m. on the day before the colonoscopy along with a clear liquid diet. The bowel clean-out was good; providing an adequate view of colon. No complaints were voiced by the patient.

View of transverse colon of Patient #6 appears at Figure 6.